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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,020	05/06/2002	Elaine Sophie Elizabeth Stokes	P 282705	5058

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WASHINGTON, DC 20004

EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
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1624

15

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/913,020

Applicant(s)

STOKES ET AL.

Examiner

Tamthom N. Truong

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 39-49, 51, 61 and 62 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 39-45, 49, 51 and 62 is/are rejected.
- 7) ☒ Claim(s) 46-48 and 61 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☒ None of:  
1. ☒ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13, 14. 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

Applicant's election of Group II (claims 39-49, and 51) in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-38, 50, and 52-60 have been cancelled, leaving claims 39-49, and 51 for consideration along with new claims 61, and 62.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Lack of Written Description** (for “*prodrug*”): Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 39 recites the limitation of “*prodrug*”, which does not have a written description in terms of the functional groups bonded to formula (II), and their location on formula (II) or its substituents. Thus, one cannot ascertain the structure of the intended “*prodrug*”.

2.     **Enablement** (for “*prodrug*”): Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 39 is not enabled for the “*prodrug*” it recites. Since the structure of the claimed “*prodrug*” cannot be determined, it would require undue experimentation to make and use such a “*prodrug*”.

3.     **Lack of Written Description:** Claims 39-45, 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 39 allows for 8, 9, 10, 12, or 13-membered bicyclic or tricyclic moiety. However, except quinoline and indoline, the specification does not describe other bicyclic or tricyclic moiety in terms of atom arrangement, and degree of saturation, as well as how the rings are fused. Thus, except quinoline and indoline, the structure of ring C is indeterminate.

4.     **Scope of Enablement:** Claims 39-45, 49, 51, and 62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation and use of compounds of formula II wherein ring C is quinolyl or indolyl, does **not** reasonably provide **enablement for the preparation and use** of compounds of formula II wherein ring C is other bicyclic or tricyclic moieties. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

**a. The breadth of the claims:** The instant claims allow for compounds of formula (II) wherein ring C can be a bicyclic [other than quinoline or indoline] or a tricyclic moiety. The specification does not describe the structural make-up for such a moiety, except quinolyl and indolyl. Thus, one cannot ascertain what other rings can constitute the intended bicyclic or tricyclic moiety.

**b. The amount of direction or guidance presented:** Not only there is no general description for a bicyclic or tricyclic moiety, there is no guidance as to how such a ring can be obtained. The generic reaction scheme on page 67 reveals a starting material of formula IV for the addition of ring C to the quinazolyl ring. However, there appears to

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be no guidance as to how formula IV can be prepared or obtained commercially. The provided examples all have ring C as either quinolyl or indolyl ring. Thus, following said examples, one can only obtain compounds of formula (II) with ring C as a quinolyl or indolyl ring, and nothing else.

Regarding the biological activity for the use, it appears that only compounds having quinolyl or indolyl ring were tested. Because each ring system has its own chemical and biological properties, the biological activity for compounds having quinolyl or indolyl ring cannot be extrapolated to compounds having other ring systems.

c. The **state of the art**, as evident by the teachings of **Myers et. al.** and **Cockerill et. al.** (cited on IDS), does not appear to teach the combination of quinazoline-(O/S)- with a bicyclic moiety other than quinoline or indoline.

Therefore, with the **unpredictable nature** of the pharmaceutical art, and limited guidance, the skilled chemist and clinician would have to carry out undue experimentation to make and use compounds of formula II with C as a ring other than quinoline or indoline.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 45, and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

d. Claim 45 lacks antecedent basis because the proviso for R<sup>2</sup> not to be “substituted or unsubstituted C<sub>1-5</sub>alkyl, halogeno, C<sub>1-5</sub>alkoxy, C<sub>2-5</sub>alkenyl, phenoxy or phenylC<sub>1-5</sub>alkoxy” does not have antecedent basis in claim 39.

e. In claim 62, the phrase “antiangiogenic or vascular permeability reducing effect” is unclear as to what diseases are directed to. Furthermore, it is not clear if claim 62 is intended as a method of treatment.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 39-41, 43, 44, 49, and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Schaper et. al.** (US 5,859,009). In Tables 9 and 10, Schaper et. al. list some substituted quinazolinyl compounds (e.g., compounds #906, #1014, #1022, #1032, etc.) that are analogous to compounds of the instant formula II with the following substituents:

- i. Ring C is a saturated, non-aromatic 10-membered bicyclic moiety;
- ii.  $R^1$  represents  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxymethyl;
- iii.  $n = 0$  or  $1$ ;
- iv.  $R^{2a}$  represents hydrogen.

The disclosed compounds differ from those claimed herein by not having a substituent on the quinazolinyl ring that corresponds to the instant variable  $R^2$ . However, on column 4, the preferred embodiment (starting from line 52) allows for a quinazoline system “*which can be substituted in the carbocyclic moiety by fluorine*” [emphasis added]. The disclosed compounds have fungicidal property, and can be used in the “hygiene field” (see column 19 lines 13-21), which suggests a topical pharmaceutical composition.

Therefore, one of the ordinary skill in the art would have been motivated to select some compounds of the instant formula II because one would have expected said compounds to have fungicidal activity as well. Thus, at the time of the invention, it would have been obvious to one skilled in the art to make and use some compounds of the instant formula II.



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***Claim Objections***

7. Claims 46-48, and 61 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims recite species that are not taught by **Schaper et. al.** (US'009) or any prior arts of record.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (7 am -12 pm, and 3 pm - 6 pm) starting from 10-1<sup>st</sup> -03).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

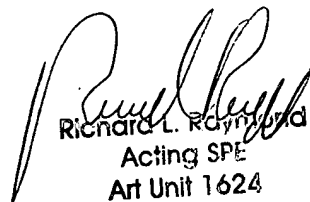
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



T. Truong

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January 7, 2004



Richard L. Raymond  
Acting SPE  
Art Unit 1624